

YPL-0089

REMARKS

In response to the office action dated March 24, 2005, Applicants respectfully request reconsideration based on the above claim amendment and the following remarks. Applicants respectfully submit that the claims as presented are in condition for allowance.

Claims 1-7 are pending in the present application. The specification has been amended to correct a typographical error, as explained in detail below. Claim 5 has also been amended to correct a typographical error, as explained in detail below. No new matter has been introduced by these amendments, and therefore, no search is required. As explained below, Applicants believe they have placed the claims in condition for allowance according to 37 C.F.R. 1.116, and respectfully request reconsideration and allowance of the claims in view of the above amendments and the following remarks.

Specification Objection

The specification stands objected to for informalities. In particular, the term "*Klebsiella pneumoniae*" is incorrectly spelled as "*Klebsiela pneumoniae*" on page 1, line 10 of the specification. Applicants respectfully replace the incorrectly spelled term "*Klebsiela pneumoniae*" with "*Klebsiella pneumoniae*".

Claim Objections

Claims 4-7 stand objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative way. Applicants respectfully traverse the objection, for claims 4-7 are in alternative form, which is allowed under 35 U.S.C. §112 in applications filed on and after January 24, 1978. MPEP §608.01(n). If Applicants' language in claims 4-7 is compared to the examples in MPEP §608.01(n), subsection A. Acceptable Multiple Dependent Claim Wording, Applicants' language is comparable to the following acceptable example:

"Claim 8. A gadget as in one of claims 4-7, in which ---".

Therefore Applicants respectfully request withdrawal of the objection to the language of claims

YPL-0089

4-7 as being in improper form.

Claim Rejections Under 35 U.S.C. §112

Claim 5 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner has stated the element 5—15 g NaPH₄ [sic] in claim 5 is unclear, and therefore, Applicants have amend Na₂PH₄, a typographical error in claim 5, to Na₂HPO₄. Applicants respectfully request reconsideration and withdrawal of the rejection of claim 5 under 35 U.S.C. § 112, second paragraph.

Claim Rejections Under 35 U.S.C. §103

Claims 1 and 4–7 stand rejected under 35 U.S.C. 103(a) as being allegedly unpatentable over Badia et al., J. Bacteriology, 1984 (hereinafter “Badia”) in view of Cameron et al., US 6,303,352 (hereinafter “Cameron”) for the reasons indicated on pages 3–5 of the Office Action. Applicants respectfully traverse this rejection for the following reasons.

The Examiner stated that Badia teaches a process of producing 1, 2-propanediol, comprising incubating *K. pneumoniae* aerobically in a medium containing 20 mM glucose and separating the 1, 2-propanediol from the culture. The Examiner has stated that Badia does not teach using the claimed range of 10-50 g/L of glucose as the carbon source. The Examiner stated that it would have been obvious to one of ordinary skill in the art to add more glucose to the reaction mixture produce more 1, 2-propanediol. Further the Examiner stated that it would have been obvious to use at least 10 g glucose/L because Cameron teach using this amount for the microbial production of 1,2-propanediol.

To establish *prima facie* obviousness of a claimed invention, three basic requirements must be met: (1) There must be some suggestion or motivation, either in the reference themselves or in the knowledge generally available to one of ordinary skill in the art to combine reference teachings; (2) There must be a reasonable expectation of success; and (3) the prior art references must teach or suggest all the claim limitations. See MPEP §2143. However,

YPL-0089

Applicants argue that the Examiner has failed to establish a *prima facie* case of obviousness, and therefore, the obviousness rejection under 35 U.S.C. §103(a) is improper for the following reasons: (1) there is no suggestion or motivation to combine Badia and Cameron and (2) there is no reasonable expectation of success of such a combination.

I. Examiner Fails To Establish a Prima Facie Case of Obviousness

A. One of Ordinary Skill in the Art Would Not Make the Combination

The mere fact that the references *can* be combined or modified does not render the resultant combination obvious unless the prior art also suggests the *desirability* of the combination. *In re Mills*, 916 F.2d 680, 16 U.S.P.Q. 2d 1430 (Fed.Cir. 1990). There is no indication of the desirability of combining Badia and Cameron, and therefore, Applicant respectfully states that the Examiner's conclusion that one of ordinary skill in the art would combine the two references is improper.

Badia indicates that 1, 2-propanediol was excreted from *K. pneumoniae* grown anaerobically on fucose or rhamnose (Seep.435, last paragraph, first sentence), but was virtually undetectable, presumably close to the limits of their detection method, when the cells grew aerobically on fucose, rhamnose, or other sugars such as glucose. (See p. 435, Col. 2, last sentence of first full ¶ and p. 436, Table 1). Specifically, Table 1 indicates that when *K. pneumoniae* grew anaerobically on fucose or rhamnose, the concentration of 1, 2-propanediol excreted was 19.6 mM and 20.0 mM respectively, and only 0.2 mM from anaerobic growth on glucose. When *K. pneumoniae* grew aerobically on fucose or rhamnose, the concentration of 1, 2-propanediol excreted was stated on p. 435 to be "virtually undetectable" at 0.2 mM and 0.4 mM, respectively (See p. 436, Table 1); aerobic growth on glucose was also stated to produce "virtually undetectable" amounts of 1,2-propanediol, presumably less than or equal to the 0.2 mM listed in Table 1 as the amount excreted under anaerobic conditions.

Further, Badia explains that propanediol oxidoreductase was induced only in fucose or rhamnose, but not in glucose, because the presence of oxygen prevents the expression of the

YPL-0089

enzyme activity. (See p. 435, Col. 2, ¶ 4 and p. 436, Table 2). In addition, Badia indicates that cross-reaction was not found with cell extracts grown under non-inducing conditions such as aerobic or anaerobic growth on glucose, and thus when glucose is used as the carbon source, propanediol oxidoreductase is not produced under both aerobic and anaerobic conditions. (See p. 346, Col. 1, ¶ 2). In sum, Badia teaches that when *K. pneumoniae* is aerobically grown on glucose, 1, 2-propanediol production is “virtually undetectable” and that a key enzyme for propanediol production is not induced in *K. pneumoniae* under aerobic growth conditions in glucose. Both of these teachings of Badia teach away from use of glucose, at any concentration, as a carbon source when growing *K. pneumoniae* for the purpose of producing 1,2-propanediol.

Based on these teachings of Badia, one of ordinary skill in the art would infer from the above that when glucose is used as the carbon source, under either aerobic or anaerobic conditions, propanediol oxidoreductase would not be produced in induced quantities, and as a result, little 1, 2-propanediol would be produced, if any. (See p. 346, Col. 1, ¶ 2). Therefore, one of ordinary skill in the art would not have the motivation, simply based on Badia alone, to add higher concentrations glucose to an aerobic growth culture of *K. pneumoniae* in the hope of obtaining higher amounts of excreted propanediol, because Badia teaches that when *K. pneumoniae* is grown aerobically, due to the limited amount of propanediol oxidoreductase, 1, 2-propanediol would not be produced even when the concentration of glucose were increased to 10g/L.

Additionally, Applicants assert that there would be no motivation for one skilled in the art to combine Badia with Cameron. As discussed above, Badia teaches away from use of glucose, at any concentration under either anaerobic or aerobic conditions, as a carbon source when growing *K. pneumoniae* for the purpose of producing 1,2-propanediol. Cameron teaches using 10g. glucose/L, but Cameron’s teachings are for the anaerobic growth of a recombinant *E. coli* strain specifically engineered to produce 1,2-propanediol when grown on glucose. Applicants can find no teaching or suggestion in Cameron that would motivate a skilled practitioner to use Cameron’s concentration 10 g glucose/L for growth of Badia’s *K. pneumoniae* to produce 1,2-propanediol in light of Badia teaching away from use of glucose under either aerobic or

YPL-0089

anaerobic growth conditions.

B. There Is No Reasonable Expectation of Success

The prior art can be combined to reject claims as *prima facie* obvious if there is a reasonable expectation of success. *In re Merck & Co., Inc.*, 800 F.2d 1091, 231 U.S.P.Q. 375 (Fed. Cir. 1986). Therefore, evidence showing no reasonable expectation of success may support a conclusion of nonobviousness. *In re Rinehart*, 531 F.2d 1048, 189 U.S.P.Q. 143 (CCPA 1976). There is no indication of a reasonable expectation of success in Badia or Cameron, and therefore, Applicant respectfully asserts that the Examiner's conclusion of obviousness is improper.

Cameron uses a triose phosphate isomerase knockout mutant of *E. coli* (*tpi*-), AA200 (col 6, lines 33-39), transformed with pSEARX containing the gene for rat lens aldose reductase (col.7, line 33-col.8, line 36); the transformed cell line is designated as AA200::pSEARX. (See Col. 11, ¶ 7 and Table 1). Cameron states that when the transformed cell line AA200::pSEARX was anaerobically fermented with 10g/L of glucose, the AA200::pSEARX produced 71 mg/L of 1, 2- propanediol. (See Col. 12, ¶1 and Table 1). Cameron teaches that yeast and other cellular hosts can also be transformed with the aldose reductase gene and can be used to produce 1,2- propanediol (col 9, lines 20-23). However, Cameron does not teach producing 1, 2- propanediol by aerobically cultivating *K. pneumoniae* on highly concentrated glucose.

Based on the teachings of Badia and Cameron, one of ordinary skill in the art would not reasonably expect that combining the teachings of Badia and Cameron to grow *K. pneumoniae* on a high concentration of glucose would successfully produce 1, 2-propanediol, because the transformed *E. coli* cell line AA200::pSEARX and *K. pneumoniae* are different species. A recombinant *E. coli* used in Cameron and the *K. pneumoniae* are different cells with the potential for differing metabolic enzyme activity levels under any given set of growth conditions.

Thus, as there is no motivation to combine the teachings of Badia with the glucose concentration of Cameron, and there is no reasonable expectation of success should the teachings of Badia be combined with the glucose concentration of Cameron, no *prima facie* case of

YPL-0089

obviousness over Badia in view of Cameron has been established.

II. *Unexpected Results*

Even if a *prima facie* case of obviousness were conceded, which it is not, it is respectfully submitted that applicant's invention is not obvious because the particular combination of claimed elements results in unexpectedly beneficial properties. An applicant can rebut a *prima facie* case of obviousness by presenting comparative test data showing that the claimed invention possesses unexpectedly improved properties or properties that the prior art does not have. *In re Dillon*, 919 F.2d 688, 692-93, 16 U.S.P.Q.2d 1987, 1901 (Fed. Cir. 1990).

A greater than expected result is an evidentiary factor pertinent to the legal conclusion of obviousness ... of the claims at issue. *See* MPEP § 716.02(a). However, a greater than additive effect is not necessarily sufficient to overcome a *prima facie* case of obviousness because such an effect can either be expected or unexpected. *See id.* To establish nonobviousness based on unexpected results, applicants must further show that the results would have been expected from the prior art to an unobvious degree and that the results have a significant advantage. *See id.*

The instant invention produced 3838 mg/L of 1, 2- propanediol from *K. Pneumoniae* culture on glucose (Example 2, pp. 4-5, Table 2), while for the recombinant *E.coli* of Cameron, only 71 mg/L of 1, 2-propanediol was produced by anaerobic fermentation using glucose (*See* Col. 12, Table 1), and for the *K pneumoniae* culture on glucose of Badia negligible amounts of 1,2-propanediol were produced at aerobic or anaerobic conditions (p.435, 1st full paragraph, last sentence and p. 436, Table 1). Therefore, the Examiner's obviousness rejection is improper because the outstanding invention produces 54-fold greater quantities of 1,2-propanediol than might be expected from the results of Cameron or Badia

Consequently, for all the foregoing reasons, Applicants request reconsideration and withdrawal of the rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Badia in view of Cameron.

YPL-0089

Conclusion

In view of the foregoing, it is respectfully submitted that the instant application is in condition for allowance. Accordingly, it is respectfully requested that this application be allowed and a Notice of Allowance issued. If the Examiner believes that a telephone conference with Applicants' attorneys would be advantageous to the disposition of this case, the Examiner is cordially requested to telephone the undersigned.

In the event the Commissioner of Patents and Trademarks deems additional fees to be due in connection with this application, Applicants' attorney hereby authorizes that such fee be charged to Deposit Account No. 06-1130.

Respectfully submitted,
CANTOR COLBURN LLP

By Sandra L. Shaner

Sandra L. Shaner
Reg. No. 47, 934
Cantor Colburn LLP
55 Griffin Road South
Bloomfield, CT 06002
Telephone (860) 286-2929
Facsimile (860) 286-0115

Date: July 25, 2005
Customer No.: 23413